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Immunotherapy of cancer with dendritic-cell-based vaccines.

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Abstract

Animal studies have shown that vaccination with genetically modified tumor cells or with dendritic cells (DC) pulsed with tumor antigens are potent strategies to elicit protective immunity in tumor-bearing animals, more potent than "conventional" strategies that have been tested in clinical settings with limited success. While both vaccination strategies are forms of cell therapy requiring complex and costly ex vivo manipulations of the patient's cells, current protocols using dendritic cells are considerably simpler and would be more widely available. Vaccination with defined tumor antigens presented by DC has obvious appeal. However, in view of the expected emergence of antigen-loss variants as well as natural immunovariation, effective vaccine formulations must contain mixtures of commonly, if not universally, expressed tumor antigens. When, or even if, such common tumor antigens will be identified cannot be, predicted, however. Thus, for the foreseeable future, vaccination with total-tumor-derived material as source of tumor antigens may be preferable to using defined tumor antigens. Vaccination with undefined tumor-derived antigens will be limited, however, by the availability of sufficient tumor tissue for antigen preparation. Because the mRNA content of single cells can be amplified, tumor mRNA, or corresponding cDNA libraries, offer an unlimited source of tumor antigens. DC transfected with tumor RNA were shown to engender potent antitumor immunity in animal studies. Thus, immunotherapy using autologous DC loaded with unfractionated tumor-derived antigens in the form of RNA emerges as a potentially powerful and broadly useful vaccination strategy for cancer patients.

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